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Toxoplasmosis associated with digital vasculitis and immunodeficiency—a dilemma in diagnosis

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Summary

We present a case of acquired toxoplasmosis associated with severe digital vasculitis—a previously unreported finding. The rise in *Toxoplasma gondii* antibody titres may have been attenuated by impaired cellular immunity, and this poses a problem for diagnosis.

KEY WORDS: Toxoplasmosis, immunodeficiency, Raynaud's phenomenon.

Case report

A previously healthy 25-year-old man presented following 4 months of night sweats, weight loss and latterly, Raynaud's phenomenon of his fingers and toes. A few weeks before the onset of symptoms he had been exposed to faecal material from lions and tigers, whilst repairing electric motors at a local circus. On admission he was unwell, with a pyrexia of 38°C. There was tender discrete axillary and inguinal lymphadenopathy and mild hepatosplenomegaly. Despite having received 2 previous BCG vaccinations, there was no skin scar.

The peripheral white blood count was $10{\cdot}1 \times 10^9$/litre (12% eosinophils). Plasma viscosity was elevated to 195 cp. Chest radiography was normal. A Paul-Bunnell test was negative. Antibodies were present to *Toxoplasma gondii* (Table 1). Acute serum was examined for a wide range of viral and bacterial pathogens including adenovirus, influenza A, *Rickettsia burneti,* cytomegalovirus, mycoplasma, *Chlamydia* spp., *Salmonella typhi* and *paratyphi* and *Brucella* spp., all of which showed insignificant titres which did not show a subsequent titre rise in convalescent samples.

The hepatitis B surface antigen was negative. Autoantibodies to DNA, smooth muscle and mitochondria were negative. Serum immunoglobulin IgA, IgG and IgM levels were 2·5 g/litre, 12·5 g/litre and 0·8 g/litre, respectively (normal). Extractable nuclear antigen, C-reactive protein, cryoglobulins, serological tests for syphilis, C1q binding, and RA latex were all negative/normal. Aortic arch and visceral angiography were normal.

TABLE 1. *Toxoplasma gondii* antibody titres

PHA	IFA	Dye test	IgM
1024*	512	256	10
2056†	1024	256	—

*Four months after start of symptoms.
†Five months after start of symptoms.
PHA = indirect haemagglutination test; IFA = indirect fluorescent test; standard criteria for acute toxoplasmosis need rising titres, and dye test titre >512[2]. IgM level is raised but low.

Specimens of liver, spleen and lymph nodes removed at laparotomy showed inconclusive features of toxoplasmosis (see Miettinen, 1981). There was no evidence of Hodgkin's disease, tuberculosis, sarcoidosis, *Histoplasma capsulatum,* leishmaniasis or *Herpes simplex* infection. A computerized tomographic (CT) scan performed 1 year later showed no evidence of a reticulosis or abdominal malignancy.

Skin testing with old tuberculin (100 units), candida antigen (10 units) and streptokinase (4 and 40 units) failed to produce a delayed reaction. Lymphocyte transformation to phytohaemagglutinin was reduced to 65% of normal. The T helper cell/suppresor cell ratio was normal at 2/1, and the T cell population was normal. Total immunoglobulins were normal.

A 6-week course of pyrimethamine 50-mg daily with sulphadiazine 500 mg 4 times daily resulted in defervescence, resolution of lymphadenopathy and hepatomegaly, an increase in weight and improve-

ment in the Raynaud's phenomenon. The toxoplasma titres remained unchanged. Shortly after cessation of this therapy his symptoms returned, but were again controlled on 2 further occasions with antibiotics. A further relapse occurred on completion of the third course. Further treatment with prednisolone 10 mg 3 times daily and azathioprine 2·5 mg/kg daily was commenced. There was again some further improvement in the Raynaud's phenomenon, but this has since recurred, with frank digital subungual haematomata and distal gangrene.

Discussion

Low antibody titres to *Toxoplasma gondii* in 60% of the U.K. population signifies prior infection. Serological diagnosis, then, of acute toxoplasmosis is said to require a high or rising titre—in particular the Sabin-Feldman dye test (Fleck and Kwantes, 1980). However, this diagnostic exactitude is only possible if the patient presents early, as titres can return to near normal—within 3 weeks in some cases (Krick and Remington, 1978). Although acute acquired toxoplasmosis is more likely to occur in immunocompromised patients, some degree of immunocompetence must be necessary to mount a high antibody titre response. A low titre consequently cannot be disregarded as insignificant in some patients who are immunocompromised. Furthermore, histology can be unhelpful—the identification of the organism in tissue may be irrelevant, and non-specific hyperplasia of lymph nodes may be the only change in toxoplasmosis (Miettinen, 1981). Our patient presented both late and with defective cellular immunity, and epitomizes the diagnostic dilemma, if the standard serological criteria are applied.

Nevertheless, the history, signs and prompt response to initial treatment and at each relapse is strong evidence for the diagnosis of acute toxoplasmosis. The fact that there was no skin scar despite 2 previous BGG vaccinations points to a pre-existing immunodeficiency rather than it being toxoplasma-induced. This latter observation also raises the possibility that the toxoplasma infection occurred as part of the acquired immunodeficiency syndrome (AIDS)—and indeed there was evidence of depressed cellular immunity in the patient, although he denied homosexual relationships.

It is pertinent that there were no other significant levels or rises in antibody titres to a wide range of pathogens tested, and it is therefore unlikely that the toxoplasma titre was an anamnestic reaction.

The onset of severe digital vasculitis in this patient may be further evidence of a disturbed immune response. A similar finding occurs following hepatitis B infection and leprosy, and although vasculitis has been described rarely in the cerebral vasculature in toxoplamosis (Vietzke *et al.*, 1968), digital vasculitis has to our knowledge not been recognized. Recently described thrombocytopenia may be another manifestation of this phenomenon (Diamant and Spirer, 1980).

There may be a group of patients who have active toxoplasmosis who for reasons of partial immunosuppression or late presentation pose a problem in diagnosis. On the one hand inappropriate treatment for toxoplasmosis carries hazards, and on the other, delay in instituting effective therapy increases morbidity and runs the risks of overwhelming disease. There is clearly a need for further evaluation of such patients and reappraisal of the serological diagnostic criteria when standard tests are used in such patients.

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